
Imaging of STAT3 signaling pathway during mouse embryonic stem cell differentiation.

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Public Summary:

Scientific Abstract:

Signal transducers and activators of transcription 3 (STAT3) is a pleiotropic transcription factor involved in a variety of physiological processes. STAT3 acts as a key transcriptional determinant of mouse embryonic stem (ES) cell self-renewal and plays a pivotal function in early mammalian embryogenesis because the development of many organs requires STAT3 activation. However, little is known about the role of STAT3 function during ES cell differentiation. To answer this question, we built a lentiviral construct with 7-repeat STAT3-binding sequence (enhancer) and minimal TA (promoter) driving renilla luciferase and monomeric red fluorescence protein (Rluc-mRFP), followed by a constitutive cytomegalovirus promoter driving green fluorescent protein as a selection marker. The specificity of our custom-designed 7-repeat STAT3 reporter construct was first confirmed by cotransfection with constitutively active version of STAT3 (STAT3C) into human embryonic kidney 293T cells. Next, a mouse ES cell line stably transduced with STAT3 reporter construct was isolated. This ES cell line showed a tight response in reporter gene expression with leukemia inhibitory factor (LIF) induction and was chosen as a developmental model for the STAT3 functional study. Using serial noninvasive bioluminescence imaging, we showed that the onset of embryoid body (EB) formation involved inhibition of STAT3 activity. However, during differentiation, STAT3 activity steadily increased from day 5 to 14 and was reduced by day 21. STAT3 activity was also confirmed separately by Western blots. Finally, phosphorylation of STAT3 was also found to correspond with cardiomyocyte differentiation. In summary, this is the first study to monitor real-time STAT3 activity during ES cell differentiation. This genetically modified line can be used to study the biological role of STAT3 during ES cell differentiation into different derivatives.

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